

## CU Index™<sup>†</sup> Testing Services

**Test Name:** CU Index™<sup>†</sup> test

**Alternate Names:** *CU Autoantibody Signature*

Autoimmune chronic urticaria test

Functional Anti-FcεR Test

**Test Code:** 2103

**CPT Code:** 86352

**Clinical Utility:** Patients with a chronic form of urticaria who are positive ( $\geq 10$ ) with the CU Index (Functional Anti-FcεR test) have an autoimmune basis for their disease. A positive result does not indicate which autoantibody (anti-IgE, anti-FcεRI or anti-FcεRII) is present. Studies with this CU Index (Functional Anti-FcεR test) indicated that 41% of the CU patients were positive for this autoantibody, which is similar to the prevalence in published studies<sup>2-6</sup>. A comparison to the Autologous Serum Skin Test (ASST) result is also shown in reference 7. The sensitivity and specificity are similar to previous reports<sup>3,6</sup>. However, it should be noted the presence of histamine releasing factors in serum may cause a positive result.

**Background For Test Application:** Chronic urticaria (CU) is a common skin disorder affecting 0.1 to 1% of the general population. It is characterized by recurrent, transitory, pruritic erythematous wheals present for at least 6 weeks<sup>1</sup>. The impact of CU on the quality of life is significant. Kaplan and others have demonstrated that in 30 – 50% of these CU patients there is an autoimmune etiology with autoantibodies against IgE, FcεRI or FcεRII (CD23)<sup>2-6</sup>. These autoantibodies are presumed to bind to the surface of mast cells and basophils initiating a signal transduction cascade that results in the secretion of histamine and other mediators. The treatment course for those with the autoimmune form of the disease is often different than for acute and transient urticaria or idiopathic chronic urticaria. Drugs that modulate the basic immunological aspects of the disease (e.g. methotrexate, calcineurin inhibitors, etc.) may be considered if an autoimmune etiology is established<sup>8,9</sup>.

### Specimen Requirements:

- A minimum volume of 1.0mL of serum is required.
- Blood should be collected and allowed to clot prior to centrifugation.
- Patients taking calcineurin inhibitors should stop their medication for 72 hours prior to draw<sup>8</sup>.
- Patients taking prednisone should stop medication for 2 weeks before blood draw.
- The specimen can be shipped via overnight courier at ambient temperature. If the specimen is to be held for more than a week, it should be stored frozen until shipped to the lab.
- Note that serum is the only acceptable specimen.

**Units and Normal Reference Range:** The result is reported as an index value. The reference range for a healthy non-CU population is less than 10. Values greater than or equal to 10 indicate that donor basophils were stimulated by patient serum to release histamine. The larger the value the more histamine released.

### Method:

1. Ex-Vivo challenge and cell culture. Donor blood cells are incubated with patient serum, a negative control and a positive control. Following the ex-vivo challenge, the cells are centrifuged and the supernatant is recovered for assay of histamine released.
2. Histamine analysis. Using a quantitative enzyme immunoassay, the histamine released into the supernatant is measured and compared to the total histamine in the basophils.

IBT Laboratories determined the performance characteristics of this test. It has not been approved or cleared by the FDA.

**Related Tests:** The following may be appropriate for some patients:

Test Code	Test Name
2105	Anti-IgE
403005	CU (Chronic Urticaria) Index™ Panel (includes all tests below)
2103	CU Index™ test
322	Anti-Thyroid Peroxidase IgG (Anti-TPO)
30055	Thyroid Stimulating Hormone (TSH)
30056	Anti-Thyroglobulin IgG (Anti-Tg)

### Selected References:

1. Greaves M. Chronic Urticaria. *J Allergy Clin Immunol.* 2000. 105(4):664-672.
2. Tong LJ, Balakrishnan G, Kochan JP, Kinet JP, and Kaplan AP. Assessment of autoimmunity in patients with chronic urticaria. *J Allergy Clin Immunol.* 1997. 99(4):461-465.
3. Ferrer M, Kinet JP, and Kaplan AP. Comparative studies of functional and binding assays for IgG anti-FcεRIα (α-subunit) in chronic urticaria. *J Allergy Clin Immunol.* 1998. 101:672-676.
4. Puccetti A, Bason C, Simeoni S, Millo E, Tinazzi E, Beri R, Peterlana D, Zanoni G, Senna G, Corrocher R, and Lunardi C. In chronic idiopathic urticaria autoantibodies against FcεRII/CD23 induce histamine release via eosinophil activation. *Clin Exp Allergy.* 2005. 35:1599-1607.
5. Soundararajan S, Kikuchi Y, Joseph K, and Kaplan AP. Functional assessment of pathogenic IgG subclasses in chronic autoimmune urticaria. *J Allergy Clin Immunol.* 2005. 115:815-21.
6. Platzer MH, Grattan CEH, Poulsen LK, and Skov PS. Validation of basophil histamine release against the autologous serum skin test and outcome of serum-induced basophil histamine release studies in a large population of chronic urticaria patients. *Allergy.* 2005 60:1152-1156.
7. Altrich ML, Halsey JF, and Altman L. Comparison of the in vivo autologous skin test with in vitro diagnostic tests for diagnosis of chronic autoimmune urticaria. *Allergy Asthma Proc.* 2009;30:28-34.
8. Marsland AM, Soundararajan S, Joseph K, and Kaplan AP. Effects of calcineurin inhibitors on an in vitro assay for chronic urticaria. *Clin Exp Allergy.* 2005. 35:554-559.
9. Grattan CEH, O'Donnell BF, Francis DM, Niimi N, Barlow RJ, Seed PT, Kobza Black A, and Greaves MW. Randomized double-blind study of cyclosporine in chronic 'idiopathic' urticaria. *British Journal of Dermatology.* 2000. 143:365-372.

<sup>†</sup>Patent pending

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***Anti IgE  
IgG Autoantibody to IgE  
IgG anti-IgE***

Test Code 2105

<b>CPT CODE</b>	83516
<b>SPECIMEN REQUIREMENT</b>	
Type:	Serum (Note: Serum is the only acceptable specimen)
Volume:	1 mL minimum
Handling:	Blood should be collected and allowed to clot prior to centrifugation. <b>NOTE:</b> Patients taking Xolair® should not be tested as they will have a false positive result on the Anti-IgE Test.
Storage:	If the specimen is to be held more than two weeks, it should be stored frozen until shipped to the lab.
Shipping:	Ship via overnight courier at ambient temperature
<b>METHODOLOGY</b>	ELISA
<b>SET-UP SCHEDULE</b>	Friday
<b>STANDARD TURNAROUND TIME</b>	1-7 business days from receipt of specimen
<b>CLINICAL UTILITY</b>	This ELISA measures IgG antibodies specific for IGE. These autoantibodies have been implicated as a causative agent in autoimmune chronic urticaria. In addition, these autoantibodies have also been implicated as significant in atopic dermatitis and hyper IgE syndrome
<b>RELATED TESTS</b>	
	403005 CU (Chronic Urticaria) Index™ Panel (Includes all tests below)
	2103 CU Index™
	322 Anti-Thyroid Peroxidase IgG (Anti-TPO)
	2004 Thyroid Stimulating Hormone (TSH)
	2005 Anti-Thyroglobulin IgG (Anti-Tg)



## Anti-Fc $\epsilon$ R1 $\alpha$ by Western Blot

Test Code: 30002

**For Research Use Only**

<b>CPT CODE</b>	
<b>SPECIMEN REQUIREMENT</b>	
Type:	Serum
Volume:	2 mL
Handling:	
Storage:	Ambient
Shipping:	No special shipping requirements
<b>METHODOLOGY</b>	Western Blot
<b>SET-UP SCHEDULE</b>	Call for set-up schedule
<b>STANDARD TURNAROUND TIME</b>	2 weeks from receipt of Specimen
<b>CLINICAL UTILITY</b>	An autoimmune etiology is involved in a number of diseases, including allergic diseases such as chronic urticaria and asthma. Auto-antibodies against IgE, Fc $\epsilon$ R1 or Fc $\epsilon$ R2 (CD23) have been linked to these diseases. These auto-antibodies are presumed to bind the high affinity IgE Fc receptor (Fc $\epsilon$ R1) on the surface of mast cells and basophils, which initiates a signal transduction cascade that results in the secretion of histamine and other mediators. These Fc $\epsilon$ R1 receptors are formed as a complex between the alpha and beta subunits, with the alpha subunit having an extracellular domain that may be targeted by auto-antibodies. In clinical and method development studies, there is a need for an autoantibody assay detecting the antibodies specific to the extracellular domain of the Fc $\epsilon$ R1 $\alpha$ . This anti-Fc $\epsilon$ R1 $\alpha$ by Western Blot assay detects IgG antibodies specific to Fc $\epsilon$ R1 $\alpha$ .